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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE REISSUE APPLICATION OF:  
FRANKS ET AL.

U.S. PATENT 5,098,893 :EXAMINER RUSSEL, J.  
(ANTICIPATED)

SERIAL NO: NEW APPLICATION  
(CONTINUATION OF 09/270,791, FILED 03/17/99)

FILED: HERWITH :GROUP ART UNIT 1653  
(ANTICIPATED)

FOR: STORAGE OF MATERIALS

Prior to examination on the merits, please amend this application as follows.

PRELIMINARY AMENDMENT

I. **IN THE CLAIMS**

Please cancel claims 1-16.

Please add the following new claims.

-- 17. A process of forming a composition which is storage-stable at 20° C, said composition comprising the steps of:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;

wherein said composition has the properties that it is storage-stable and exists in said

glassy state when at 20° C;

wherein said composition contains no more than 4 percent by weight of water;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;

wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said step of forming comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C.

18. The process of claim 17 wherein said step of forming comprises maintaining a sub atmospheric pressure on the combined carrier substance and purified biologically active material while heating the combination to at least 30° C and not exceeding 80° C.

19. The process of claim 17 wherein said carrier substance comprises a water soluble or water swellable synthetic polymer.

20. The process of claim 17 wherein said purified biologically active material is not an enzyme.

21. The process of claim 17 wherein said purified biologically active material is not rennin.

22. The process of claim 17 wherein said purified biologically active material comprises a hormone.

23. The process of claim 17 wherein said purified biologically active material comprises immunoglobulin.

24. The process of claim 17 wherein said purified biologically active material comprises a blood clotting factor.

25. The process of claim 17 wherein said purified biologically active material comprises a pharmacologically active protein.

26. A glassy state composition which is storage-stable at 20° C, comprising:

- (1) a carrier substance which is water-soluble or water-swellable and
- (2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1.

27. The composition of claim 26 wherein said composition contains no more than four weight percent water.

28. The composition of claim 26 wherein said ratio is about 2:1.

29. The composition of claim 26 wherein said ratio is about 1:1.

30. The composition of claim 26 wherein said biologically active material is not an

enzyme.

31. The composition of claim 26 wherein said biologically active material is not rennin.

32. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1.

33. The method of claim 32 wherein said weight ratio is about 1:1.

34. The method of claim 32 wherein said weight ratio is about 1:2.

35. The method of claim 32 wherein said composition contains no more than 4 weight

percent water.

36. The method of claim 32 wherein said biologically active material is not an enzyme.
37. The method of claim 32 wherein said biologically active material is not rennin.
38. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7.

39. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

40. A composition which is storage-stable at 20° C, comprising:

- (1) a carrier substance which is water-soluble or water-swellable;
- (2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not an enzyme.

41. A composition which is storage-stable at 20° C, comprising:
- (1) a carrier substance which is water-soluble or water-swellable and
  - (2) at least one material to be stored which is dissolved in said carrier substance;
- wherein said composition has the property that it exists in a glassy state when at 20° C;
- wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
- wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
- wherein said composition contains no more than 4 percent by weight of water; and
- wherein said biologically active material is not rennin.
42. A composition which is storage-stable at 20° C, comprising:
- (1) a carrier substance which is water-soluble or water-swellable and
  - (2) at least one material to be stored which is dissolved in said carrier substance;
- wherein said composition has the property that it exists in a glassy state when at 20° C;
- wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
- wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
- wherein said biologically active material is not an enzyme; and

wherein said carrier substance does not comprise maltotriose.

43. A composition which is storage-stable at 20° C, comprising:

- (1) a carrier substance which is water-soluble or water-swellable and
  - (2) at least one material to be stored which is dissolved in said carrier substance;
- wherein said composition has the property that it exists in a glassy state when at 20° C;  
wherein said at least one material comprises a purified biologically active material that is  
unstable in aqueous solution at 20° C;
- wherein said biologically active material is selected from the group consisting of  
peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides,  
enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one  
or more additional moieties bound thereto; and

wherein said biologically active material is not an enzyme and is not freeze stable.

44. A method of forming a composition which is storage-stable at 20° C, comprising  
the steps of:

- (1) dissolving to form an aqueous solution
    - (a) a carrier substance which is water-soluble or water-swellable and
    - (b) at least one material to be stored;
- forming said solution into a glassy state composition by evaporating liquid water;  
wherein said composition has the property that it exists in a glassy state when at 20° C;  
wherein said at least one material comprises a purified biologically active material that is  
unstable in aqueous solution at 20° C;
- wherein said biologically active material is selected from the group consisting of  
peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides,

enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said biologically active material is not an enzyme; and

wherein said carrier substance does not comprise maltotriose. - -

II. **REMARKS**

**A. Claim Status**

Claims 17-40 are presented. Some of these claims correspond to claims rejected in the parent application. Some claims contain newly presented limitations. Rennin, which is specifically excluded by some claims, is not disclosed in the specification.

**B. Support for Presented Claims**

The following section shows support for the claims.

17. A process of forming a composition which is storage-stable at 20° C, said composition comprising the steps of:

(1) dissolving to form an aqueous solution  
(a) a carrier substance which is water-soluble or water-swellable and  
(b) at least one material to be stored;

(2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;

wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;

wherein said composition contains no more than 4 percent by weight of water;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;

wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional

Claims 1 and 12.  
Column 3 lines 1-13.

Column 2 line 41.

Claims 1, 2, and 12.  
Column 3 lines 1-13.

moieties bound thereto; and

wherein said step of forming comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C.

18. The process of claim 17 wherein said step of forming comprises maintaining a sub atmospheric pressure on the combined carrier substance and purified biologically active material while heating the combination to at least 30° C and not exceeding 80° C.

19. The process of claim 17 wherein said carrier substance comprises a water soluble or water swellable synthetic polymer.

20. The process of claim 17 wherein said purified biologically active material is not an enzyme.

21. The process of claim 17 wherein said purified biologically active material is not rennin.

22. The process of claim 17 wherein said purified biologically active material comprises a hormone.

23. The process of claim 17 wherein said purified biologically active material comprises immunoglobulin.

24. The process of claim 17 wherein said purified biologically active material comprises a blood clotting factor.

25. The process of claim 17 wherein said purified biologically active material comprises a pharmacologically active protein.

Column 6 lines 22-24.

Column 6 lines 22-24 and 42.

Column 3 lines 65-66.

Claims 1, 2, and 12.  
Column 3 lines 1-13.

Claims 1, 2, and 12.  
Column 3 lines 1-13.  
Rennin is not specifically disclosed.

Support for limitations presented for claim 17.

26. A glassy state composition which is storage-stable at 20° C, comprising:

- (1) a carrier substance which is water-soluble or water-swellable and
- (2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1.

27. The composition of claim 26 wherein said composition contains no more than four weight percent water.

28. The composition of claim 26 wherein said ratio is about 2:1.

29. The composition of claim 26 wherein said ratio is about 1:1.

30. The composition of claim 26 wherein said biologically active material is not an enzyme.

31. The composition of claim 26

Claim 1, and see claim 17 herein.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

Column 2 line 41.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

See claim 20.

See claim 21.

wherein said biologically active material is not rennin.

32. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

- (a) said material and
- (b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1.

33. The method of claim 32 wherein said weight ratio is about 1:1.

34. The method of claim 32 wherein said weight ratio is about 1:2.

35. The method of claim 32 wherein said composition contains no more than 4 weight percent water.

Claim 12.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

See claim 17.

36. The method of claim 32 wherein said biologically active material is not an enzyme. See claim 20.
37. The method of claim 32 wherein said biologically active material is not rennin. See claim 21.
38. A method of forming a composition which is storage-stable at 20° C, said composition comprising:  
(1) dissolving to form an aqueous solution  
    (a) a carrier substance which is water-soluble or water-swellable and  
    (b) at least one material to be stored;  
(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;  
    wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;  
    wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and  
    wherein said composition contains no more than 4 percent by weight of water; and  
    wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7.

Examples 5 at column 10 line 17; example 6 at column 11 line 7; example 7 column 11 lines 30-34; example 8 lines 40-41; example 9 column 11 last line; example 10 column 12 line 23; example 11 column 12 line 40-43; example 12 column 12 lines 56-57 and 60; example 13 column 13 lines 5-7.

39. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

See previous claims.

40. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not an enzyme.

See previous claims.

41. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides,

nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

See previous claims.

42. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and  
(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said biologically active material is not an enzyme; and

wherein said carrier substance does not comprise maltotriose.

See previous claims.

43. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and  
(2) at least one material to be stored which is dissolved in said carrier substance;  
wherein said composition has the

Table in column 13.

See previous claims.

property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said biologically active material is not an enzyme

See previous claims.

and is not freeze stable.

Column 1 lines 51.

44. A method of forming a composition which is storage-stable at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and  
(b) at least one material to be stored; forming said solution into a glassy state composition by evaporating liquid water;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or

more additional moieties bound thereto;  
wherein said biologically active  
material is not an enzyme; and

wherein said carrier substance does  
not comprise maltotriose

Table in column 13.

Respectfully submitted,

  
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